

L Number	Hits	Search Text	DB	Time stamp
1	1	"20020051786"	USPAT; US-PGPUB	2004/05/02 19:49
2	2	"6602857"	USPAT; US-PGPUB	2004/05/02 19:50
3	5	"6261840"	USPAT; US-PGPUB	2004/05/02 19:51
4	0	"6261840" and (p85\$2 or p50\$2 or p55\$2)	USPAT; US-PGPUB	2004/05/02 19:53
5	4	"6261840" and (kinase)	USPAT; US-PGPUB	2004/05/02 19:53
6	311	ptp1b	USPAT; US-PGPUB	2004/05/02 19:53
7	6	ptp1b same (p85\$2 or p50\$2 or p55\$2)	USPAT; US-PGPUB	2004/05/02 19:54

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 JAN 27 Source of Registration (SR) information in REGISTRY updated and searchable  
NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in CA/CAplus  
NEWS 5 FEB 05 German (DE) application and patent publication number format changes  
NEWS 6 MAR 03 MEDLINE and LMEDLINE reloaded  
NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
NEWS 8 MAR 03 FRANCEPAT now available on STN  
NEWS 9 MAR 29 Pharmaceutical Substances (PS) now available on STN  
NEWS 10 MAR 29 WPIFV now available on STN  
NEWS 11 MAR 29 No connect hour charges in WPIFV until May 1, 2004  
NEWS 12 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA  
NEWS 13 APR 26 PROMT: New display field available  
NEWS 14 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field available  
NEWS 15 APR 26 LITALERT now available on STN  
NEWS 16 APR 27 NLDB: New search and display fields available

NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004

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=> s PTP1b or phosphatase (w) 1b  
L1 1879 PTP1B OR PHOSPHATASE (W) 1B

=> s 11 and (mice or mouse or rat or animal or mammal or dog#)  
L2 618 L1 AND (MICE OR MOUSE OR RAT OR ANIMAL OR MAMMAL OR DOG#)

=> s 12 and (p50? or p85? or p55?)  
L3 17 L2 AND (P50? OR P85? OR P55?)

=> dup rem 13  
PROCESSING COMPLETED FOR L3  
L4 10 DUP REM L3 (7 DUPLICATES REMOVED)

=> d 1-10 ti

L4 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
TI Stearoyl-CoA desaturase 1 deficiency elevates insulin-signaling components and down-regulates protein-tyrosine **phosphatase 1B** in muscle

L4 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
TI **Mouse** models of diabetes mellitus

L4 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
TI **PTP1B** antisense-treated **mice** show regulation of genes involved in lipogenesis in liver and fat

L4 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Methods for identifying compounds that inhibit or reduce **PTP1B** (protein tyrosine **phosphatase 1B**) expression

L4 ANSWER 5 OF 10 MEDLINE on STN DUPLICATE 2  
TI **PTP1B** antisense oligonucleotide lowers **PTP1B** protein, normalizes blood glucose, and improves insulin sensitivity in diabetic **mice**.

L4 ANSWER 6 OF 10 MEDLINE on STN DUPLICATE 3  
TI Protein tyrosine **phosphatase 1B** reduction regulates adiposity and expression of genes involved in lipogenesis.

L4 ANSWER 7 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI **PTP1B** reduction regulates adiposity and expression of genes involved in lipogenesis in ob/ob **mice**.

L4 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Protein tyrosine **phosphatase-1B** negatively regulates insulin signaling in L6 myocytes and Fao hepatoma cells.

L4 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Inhibition of **PTP1B** induces differential expression of PI3-kinase regulatory subunit (**p85alpha**) isoforms.

L4 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI PTP-1B antisense modulates key elements of the insulin signaling cascade in liver and fat.

=> d 9 bib ab

L4 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:472886 BIOSIS  
DN PREV200100472886

TI Inhibition of **PTP1B** induces differential expression of PI3-kinase regulatory subunit (**p85alpha**) isoforms.  
AU Rondinone, Cristina M. [Reprint author]; Trevillyan, James M. [Reprint author]; Clampit, Jill [Reprint author]; Koterski, Sandra [Reprint author]; Zinker, Bradley [Reprint author]; Jirousek, Michael R. [Reprint author]  
CS Abbott Park, IL, USA  
SO Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A400. print.  
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001.  
CODEN: DIAEAZ. ISSN: 0012-1797.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 10 Oct 2001  
Last Updated on STN: 25 Feb 2002

=> d 10 bib ab

L4 ANSWER 10 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:441633 BIOSIS  
DN PREV200100441633  
TI PTP-1B antisense modulates key elements of the insulin signaling cascade in liver and fat.  
AU Rondinone, Cristina M. [Reprint author]; Clampit, Jill; Gum, Rebecca; Koterski, Sandra; Gaede, Lori; Waring, Jeffrey F.; Kroeger, Paul; Reilly, Regina M.; Frost, Leigh; Zinker, Bradley; Butler, Madeline; Murray, Susan; McKay, Robert; Bhanot, Sanjay; Monia, Brett; Jirousek, Michael R.; Trevillyan, James M.  
CS Abbott Park, IL, USA  
SO Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A292. print.  
Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American Diabetes Association.  
CODEN: DIAEAZ. ISSN: 0012-1797.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 19 Sep 2001  
Last Updated on STN: 23 Feb 2002

=> d 8 bib bab

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L4 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2001:472888 BIOSIS  
DN PREV200100472888  
TI Protein tyrosine **phosphatase-1B** negatively regulates insulin signaling in L6 myocytes and Fao hepatoma cells.  
AU Egawa, Katsuya [Reprint author]; Maegawa, Hiroshi; Shimizu, Shinya; Morino, Katsutaro; Bryer-Ash, Michael; Cheung, Anthony T.; Kolls, Jay K.; Kashiwagi, Atsunori; Kikkawa, Ryuichi  
CS Otsu, Shiga, Japan  
SO Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A401. print.

Meeting Info.: 61st Scientific Sessions of the American Diabetes Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001.  
CODEN: DIAEAEZ. ISSN: 0012-1797.  
DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LA English  
ED Entered STN: 10 Oct 2001  
Last Updated on STN: 23 Feb 2002

=> d his

(FILE 'HOME' ENTERED AT 21:00:44 ON 02 MAY 2004)

FILE 'MEDLINE, BIOSIS, CAPLUS, ESBIOBASE' ENTERED AT 21:01:00 ON 02 MAY 2004

L1 1879 S PTP1B OR PHOSPHATASE (W) 1B  
L2 618 S L1 AND (MICE OR MOUSE OR RAT OR ANIMAL OR MAMMAL OR DOG#)  
L3 17 S L2 AND (P50? OR P85? OR P55?)  
L4 10 DUP REM L3 (7 DUPLICATES REMOVED)

=> s l2 and py<2002  
2 FILES SEARCHED...  
L5 344 L2 AND PY<2002

=> s l5 and inhibit?  
L6 201 L5 AND INHIBIT?

=> dup rem 16  
PROCESSING COMPLETED FOR L6  
L7 105 DUP REM L6 (96 DUPLICATES REMOVED)

=> d 1-105 ti

L7 ANSWER 1 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI RNA interference mediated **inhibition** of gene expression using chemically modified short interfering nucleic acid

L7 ANSWER 2 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI RNA interference-mediated **inhibition** of protein tyrosine **phosphatase-1B** (PTP-1B) gene expression using short interfering nucleic acids

L7 ANSWER 3 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Antisense modulation of **PTP1B** (protein tyrosine **phosphatase 1B**) expression and treatment of diabetes, obesity, and cancer

L7 ANSWER 4 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
TI Nucleic acid-based ribozyme and DNAzyme modulators of gene expression

L7 ANSWER 5 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Antisense modulation of **PTP1B** expression

L7 ANSWER 6 OF 105 MEDLINE on STN DUPLICATE 2  
TI TYK2 and JAK2 are substrates of protein-tyrosine **phosphatase 1B**.

L7 ANSWER 7 OF 105 MEDLINE on STN DUPLICATE 3  
TI Acquisition of a specific and potent **PTP1B inhibitor** from a novel combinatorial library and screening procedure.

L7 ANSWER 8 OF 105 MEDLINE on STN DUPLICATE 4  
TI Galpha(i2) enhances insulin signaling via suppression of protein-tyrosine phosphatase 1B.

L7 ANSWER 9 OF 105 MEDLINE on STN DUPLICATE 5  
TI Enhanced sensitivity of insulin-resistant adipocytes to vanadate is associated with oxidative stress and decreased reduction of vanadate (+5) to vanadyl (+4).

L7 ANSWER 10 OF 105 MEDLINE on STN DUPLICATE 6  
TI Insulin stimulates tyrosine phosphorylation and inactivation of protein-tyrosine phosphatase 1B in vivo.

L7 ANSWER 11 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Potentiation of insulin-related signal transduction by a novel protein-tyrosine phosphatase **inhibitor**, Et-3,4-dephostatin, on cultured 3T3-L1 adipocytes

L7 ANSWER 12 OF 105 MEDLINE on STN DUPLICATE 7  
TI Attenuation of adhesion-dependent signaling and cell spreading in transformed fibroblasts lacking protein tyrosine phosphatase-1B.

L7 ANSWER 13 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI The reciprocal role of Egr-1 and Sp family proteins in regulation of the PTP1B promoter in response to the p210 Bcr-Abl oncoprotein-tyrosine kinase

L7 ANSWER 14 OF 105 MEDLINE on STN  
TI Insulin-stimulated hydrogen peroxide reversibly **inhibits** protein-tyrosine phosphatase 1b in vivo and enhances the early insulin action cascade.

L7 ANSWER 15 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Steric hindrance as a basis for structure-based design of selective **inhibitors** of protein-tyrosine phosphatases.

L7 ANSWER 16 OF 105 MEDLINE on STN  
TI Small molecule peptidomimetics containing a novel phosphotyrosine bioisostere **inhibit** protein tyrosine phosphatase 1B and augment insulin action.

L7 ANSWER 17 OF 105 MEDLINE on STN DUPLICATE 8  
TI Sodium stibogluconate is a potent **inhibitor** of protein tyrosine phosphatases and augments cytokine responses in hemopoietic cell lines.

L7 ANSWER 18 OF 105 MEDLINE on STN  
TI Phosphorylation of PTP1B at Ser(50) by Akt impairs its ability to dephosphorylate the insulin receptor.

L7 ANSWER 19 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Use of an anaerobic environment to preserve the endogenous activity of protein-tyrosine phosphatases isolated from intact cells.

L7 ANSWER 20 OF 105 MEDLINE on STN DUPLICATE 9  
TI Modulation of PKCdelta tyrosine phosphorylation and activity in salivary and PC-12 cells by Src kinases.

L7 ANSWER 21 OF 105 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN  
TI Modulation of PKC $\delta$  tyrosine phosphorylation and activity in salivary and PC-12 cells by Src kinases

L7 ANSWER 22 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Transcriptional regulation by BDNF using microarrays and single cell analysis in synaptic plasticity.

L7 ANSWER 23 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Role of protein tyrosine phosphorylation in acetaldehyde-induced disruption of epithelial tight junctions

L7 ANSWER 24 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Protein tyrosine phosphatase (PTP) **inhibition** by phosphomolybdate and phosphotungstate in vitro.

L7 ANSWER 25 OF 105 MEDLINE on STN  
TI Low M(r) protein tyrosine phosphatase **inhibits** growth and migration of vascular smooth muscle cells induced by platelet-derived growth factor.

L7 ANSWER 26 OF 105 MEDLINE on STN DUPLICATE 10  
TI Adenovirus-mediated overexpression and stimulation of the human angiotensin II type 2 receptor in porcine cardiac fibroblasts does not modulate proliferation, collagen I mRNA expression and ERK1/ERK2 activity, but **inhibits** protein tyrosine phosphatases.

L7 ANSWER 27 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI 1,1-Disubstituted methoxyimino acetic acid (A-119505), a novel **PTP1B inhibitor** with anti-diabetic effects in ob/ob **mice**.

L7 ANSWER 28 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Modulation of protein kinase signaling by protein phosphatases and **inhibitors**.

L7 ANSWER 29 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI cDNA microarray analysis of multidrug resistance: doxorubicin selection produces multiple defects in apoptosis signaling pathways

L7 ANSWER 30 OF 105 MEDLINE on STN DUPLICATE 11  
TI Protein tyrosine phosphatases: prospects for therapeutics.

L7 ANSWER 31 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI (2R)-2-(2',6'-dichloro-4'-dibenzo(b,d)furan-4''-ylphenoxy)-3-phenylpropanoic acid (A-321842) as a protein tyrosine **phosphatase 1B (PTP1B) inhibitor** with anti-diabetic effects in ob/ob **mice**.

L7 ANSWER 32 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Protein tyrosine **phosphatase-1B** negatively regulates insulin signaling in L6 myocytes and Fao hepatoma cells.

L7 ANSWER 33 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI **Inhibition** of **PTP1B** induces differential expression of PI3-kinase regulatory subunit (p85alpha) isoforms.

L7 ANSWER 34 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Insulin-stimulated generation of hydrogen peroxide reversibly **inhibits PTP1B** in vivo and enhances the early insulin action cascade.

L7 ANSWER 35 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 12  
TI Enhancement of post-receptor insulin signaling by trivalent chromium in hepatoma cells is associated with differential **inhibition** of specific protein-tyrosine phosphatases.

L7 ANSWER 36 OF 105 MEDLINE on STN  
TI Development of a robust scintillation proximity assay for protein tyrosine phosphatase 1B using the catalytically inactive (C215S) mutant.

L7 ANSWER 37 OF 105 MEDLINE on STN DUPLICATE 13  
TI Protein-tyrosine phosphatase 1B (PTP1B): a novel therapeutic target for type 2 diabetes mellitus, obesity and related states of insulin resistance.

L7 ANSWER 38 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Pulling strings below the surface: Hormone receptor signaling through inhibition of protein tyrosine phosphatases.

L7 ANSWER 39 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Antisense therapy for diabetes

L7 ANSWER 40 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Inhibition of protein phosphatase activity enhances hepatic insulin signaling and reverses apoB overproduction in an insulin resistant hamster model.

L7 ANSWER 41 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Methods of making protein tyrosine phosphatase-1b (PTP-1B) deficient mice and their uses in drug screening for obesity and diabetes therapy

L7 ANSWER 42 OF 105 MEDLINE on STN DUPLICATE 14  
TI A cytosolic protein-tyrosine phosphatase PTP1B specifically dephosphorylates and deactivates prolactin-activated STAT5a and STAT5b.

L7 ANSWER 43 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Down-regulation of insulin signaling by protein-tyrosine phosphatase 1B is mediated by an N-terminal binding region.

L7 ANSWER 44 OF 105 MEDLINE on STN DUPLICATE 15  
TI Overexpression of protein-tyrosine phosphatase-1B in adipocytes inhibits insulin-stimulated phosphoinositide 3-kinase activity without altering glucose transport or Akt/Protein kinase B activation.

L7 ANSWER 45 OF 105 MEDLINE on STN  
TI Residue 259 is a key determinant of substrate specificity of protein-tyrosine phosphatases 1B and alpha.

L7 ANSWER 46 OF 105 MEDLINE on STN DUPLICATE 16  
TI Structure-based design of a low molecular weight, nonphosphorus, nonpeptide, and highly selective inhibitor of protein-tyrosine phosphatase 1B.

L7 ANSWER 47 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Pleiotropic resistance to DNA-interactive drugs is associated with increased expression of genes involved in DNA replication, repair, and stress response. [Erratum to document cited in CA134:269]

L7 ANSWER 48 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Pleiotropic resistance to DNA-interactive drugs is associated with increased expression of genes involved in DNA replication, repair, and stress response

L7 ANSWER 49 OF 105 MEDLINE on STN DUPLICATE 17

TI Synthesis and **PTP1B inhibition** of novel 4-aryl-1-oxa-9-thiacyclopenta[b]fluorenes.

L7 ANSWER 50 OF 105 MEDLINE on STN DUPLICATE 18  
TI Novel benzofuran and benzothiophene biphenyls as **inhibitors** of protein tyrosine **phosphatase 1B** with antihyperglycemic properties.

L7 ANSWER 51 OF 105 MEDLINE on STN DUPLICATE 19  
TI New azolidinediones as **inhibitors** of protein tyrosine **phosphatase 1B** with antihyperglycemic properties.

L7 ANSWER 52 OF 105 MEDLINE on STN DUPLICATE 20  
TI Protein tyrosine **phosphatase-1B** in diabetes.

L7 ANSWER 53 OF 105 MEDLINE on STN DUPLICATE 21  
TI Elevated expression and activity of protein-tyrosine **phosphatase 1B** in skeletal muscle of insulin-resistant type II diabetic Goto-Kakizaki rats.

L7 ANSWER 54 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI **Inhibition** of protein tyrosine phosphatases by low-molecular-weight S-nitrosothiols and S-nitrosylated human serum albumin.

L7 ANSWER 55 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI **PTP1B inhibition** and antihyperglycemic activity in the ob/ob **mouse** model of novel 11-arylbenzo[b]naphtho[2,3-d]furans and 11-arylbenzo[b]naphtho[2,3-d]thiophenes

L7 ANSWER 56 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Small-molecule **inhibitors** of **PTP1B**.

L7 ANSWER 57 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Design and synthesis of selective PTPase 1B **inhibitors** targeted to the treatment of type II diabetes.

L7 ANSWER 58 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Small-molecule **inhibitors** of **PTP1B**.

L7 ANSWER 59 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of (2-acylaminothiazole-4-yl)acetic acid derivatives for treating metabolic disorders related to insulin resistance or hyperglycemia

L7 ANSWER 60 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of bicyclic heterocyclic amides as modulators of protein tyrosine phosphatases (PTPases)

L7 ANSWER 61 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of thieno[2,3-c]pyrans and thieno[2,3-c]pyridines as modulators of protein tyrosine phosphatases (PTPases)

L7 ANSWER 62 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of thiophenecarboxylic acid derivatives and analogs as modulators of protein tyrosine phosphatases (PTPases)

L7 ANSWER 63 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of oxallylaminothiophene derivatives as modulators of protein tyrosine phosphatases (PTPases)

L7 ANSWER 64 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Preparation of (oxallylamino)benzoic acid derivatives and analogs as

modulators of protein tyrosine phosphatases (PTPases)

L7 ANSWER 65 OF 105 MEDLINE on STN  
TI Evidence for a calpeptin-sensitive protein-tyrosine phosphatase upstream of the small GTPase Rho. A novel role for the calpain **inhibitor** calpeptin in the **inhibition** of protein-tyrosine phosphatases.

L7 ANSWER 66 OF 105 MEDLINE on STN DUPLICATE 22  
TI **PTP1B inhibition** and antihyperglycemic activity in the ob/ob **mouse** model of novel 11-arylbenzo[b]naphtho[2,3-d]furans and 11-arylbenzo[b]naphtho[2,3-d]thiophenes.

L7 ANSWER 67 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI New clues found to diabetes and obesity.

L7 ANSWER 68 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI NO alters cell shape and motility in aortic smooth muscle cells via protein tyrosine **phosphatase 1B** activation.

L7 ANSWER 69 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Differential expression and translocation of protein tyrosine **phosphatase 1B**-related proteins in ME-180 tumor cells expressing apoptotic sensitivity and resistance to tumor necrosis factor: potential interaction with epidermal growth factor receptor

L7 ANSWER 70 OF 105 MEDLINE on STN DUPLICATE 23  
TI Role of protein tyrosine **phosphatase-1B** in diabetes and obesity.

L7 ANSWER 71 OF 105 MEDLINE on STN DUPLICATE 24  
TI A phosphotyrosyl mimetic peptide reverses impairment of insulin-stimulated translocation of GLUT4 caused by overexpression of **PTP1B** in **rat** adipose cells.

L7 ANSWER 72 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 25  
TI Opening of ATP-sensitive K<sup>+</sup> channel by pinacidil requires serine/threonine phosphorylation in **rat** ventricular myocytes.

L7 ANSWER 73 OF 105 MEDLINE on STN DUPLICATE 26  
TI Overexpression of protein tyrosine phosphatase-alpha (PTP-alpha) but not PTP-kappa **inhibits** translocation of GLUT4 in **rat** adipose cells.

L7 ANSWER 74 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Substrate-trapping protein tyrosine phosphatase mutants for identification of tyrosine-phosphorylated protein substrates and their clinical uses

L7 ANSWER 75 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Reversible inactivation of protein-tyrosine **phosphatase 1B** in A431 cells stimulated with epidermal growth factor

L7 ANSWER 76 OF 105 MEDLINE on STN DUPLICATE 27  
TI Protein tyrosine phosphatase **PTP1B** suppresses p210 bcr-abl-induced transformation of **rat-1** fibroblasts and promotes differentiation of K562 cells.

L7 ANSWER 77 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Insulin regulates the dynamic balance between Ras and Rap1 signaling by coordinating the assembly states of the Grb2-SOS and CrkII-C3G complexes

L7 ANSWER 78 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Tyrosine phosphorylation of selected secretory carrier membrane proteins,

SCAMP1 and SCAMP3, and association with the EGF receptor.

L7 ANSWER 79 OF 105 MEDLINE on STN DUPLICATE 28  
TI Potent non-peptidyl **inhibitors** of protein tyrosine phosphatase 1B.

L7 ANSWER 80 OF 105 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V. on STN  
TI High glucose-induced abnormal epidermal growth factor signaling

L7 ANSWER 81 OF 105 MEDLINE on STN DUPLICATE 29  
TI Transformation suppression by protein tyrosine **phosphatase 1B** requires a functional SH3 ligand.

L7 ANSWER 82 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Multiple phosphorylation of chicken protein tyrosine phosphatase 1 and human protein tyrosine **phosphatase 1B** by casein kinase II and p60c-src in vitro

L7 ANSWER 83 OF 105 MEDLINE on STN DUPLICATE 30  
TI Protein tyrosine **phosphatase 1B** negatively regulates integrin signaling.

L7 ANSWER 84 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Method and phosphopeptides for treatment of insulin resistance based on the association of protein tyrosine **phosphatase 1B** with the activated insulin receptor

L7 ANSWER 85 OF 105 MEDLINE on STN DUPLICATE 31  
TI Protein-tyrosine phosphatases **PTP1B** and **syp** are modulators of insulin-stimulated translocation of GLUT4 in transfected **rat** adipose cells.

L7 ANSWER 86 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Phosphorylation of protein-tyrosine phosphatase PTP-1B on identical sites suggests activation of a common signaling pathway during mitosis and stress response in mammalian cells

L7 ANSWER 87 OF 105 MEDLINE on STN DUPLICATE 32  
TI Mitogen-activated protein kinase phosphatase 1 **inhibits** the stimulation of gene expression by hypertrophic agonists in cardiac myocytes.

L7 ANSWER 88 OF 105 MEDLINE on STN DUPLICATE 33  
TI Effect of tumor necrosis factor-alpha on the phosphorylation of tyrosine kinase receptors is associated with dynamic alterations in specific protein-tyrosine phosphatases.

L7 ANSWER 89 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Protein-tyrosine **phosphatase 1B** is a negative regulator of insulin- and insulin-like growth factor-I-stimulated signaling.

L7 ANSWER 90 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Protein tyrosine **phosphatase 1B** interacts with the activated insulin receptor.

L7 ANSWER 91 OF 105 MEDLINE on STN DUPLICATE 34  
TI Reciprocal modulation of ATP-sensitive K<sup>+</sup> channel activity in **rat** ventricular myocytes by phosphorylation of tyrosine and serine/threonine residues.

L7 ANSWER 92 OF 105 MEDLINE on STN DUPLICATE 35

TI Structural basis for **inhibition** of receptor protein-tyrosine phosphatase-alpha by dimerization.

L7 ANSWER 93 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Cloning and characterization of a chicken protein tyrosine phosphatase, CPTP1

L7 ANSWER 94 OF 105 MEDLINE on STN DUPLICATE 36  
TI Osmotic loading of neutralizing antibodies demonstrates a role for protein-tyrosine **phosphatase 1B** in negative regulation of the insulin action pathway.

L7 ANSWER 95 OF 105 MEDLINE on STN DUPLICATE 37  
TI Thiazolidine derivatives ameliorate high glucose-induced insulin resistance via the normalization of protein-tyrosine phosphatase activities.

L7 ANSWER 96 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 38  
TI Differentiation of peptide molecular recognition by phospholipase C-gamma-1 Src homology-2 domain and a mutant Tyr phosphatase **PTP1b**-C215S.

L7 ANSWER 97 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI The crystal structure of a low-molecular-weight phosphotyrosine protein phosphatase.

L7 ANSWER 98 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Selected molecular targets for diagnosis and therapy of epithelial ovarian cancer

L7 ANSWER 99 OF 105 MEDLINE on STN DUPLICATE 39  
TI Sequence specificity in recognition of the epidermal growth factor receptor by protein tyrosine **phosphatase 1B**.

L7 ANSWER 100 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Increased expression of specific protein tyrosine phosphatases in human breast epithelial cells neoplastically transformed by the neu oncogene.

L7 ANSWER 101 OF 105 MEDLINE on STN DUPLICATE 40  
TI Comparison of the biochemical and biological functions of tyrosine phosphatases from fission yeast, budding yeast and **animal** cells.

L7 ANSWER 102 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI Identification of a protein-tyrosine phosphatase from human platelet membranes by an immobilon-based solid phase assay.

L7 ANSWER 103 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Identification of a **rat** liver protein-tyrosine phosphatase similar to human placental PTPase-1B using quantitatively phosphorylated protein substrates

L7 ANSWER 104 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
TI Serine phosphorylation of protein tyrosine phosphatase (**PTP1B**) in HeLa cells in response to analogs of cAMP or diacylglycerol plus okadaic acid

L7 ANSWER 105 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
TI PURIFICATION AND CHARACTERIZATION OF A HIGHER-MOLECULAR-MASS FORM OF PROTEIN PHOSPHOTYROSINE PHOSPHATE PTP 1B FROM PLACENTAL MEMBRANES.

L7 ANSWER 27 OF 105 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN  
 AN 2001:449086 BIOSIS  
 DN PREV200100449086  
 TI 1,1-Disubstituted methoxyimino acetic acid (A-119505), a novel  
**PTP1B inhibitor** with anti-diabetic effects in ob/ob  
**mice**.  
 AU Liu, Gang [Reprint author]; Bai, Hao [Reprint author]; Zinker, Bradley  
 [Reprint author]; Xie, Nancy [Reprint author]; Nyugen, Bach [Reprint  
 author]; Comess, Kenneth [Reprint author]; Ballaron, Steve [Reprint  
 author]; Arnold, William [Reprint author]; Jirousek, Michael R. [Reprint  
 author]  
 CS Abbott Park, IL, USA  
 SO Diabetes, (June, 2001) Vol. 50, No. Supplement 2, pp. A506. print.  
 Meeting Info.: 61st Scientific Sessions of the American Diabetes  
 Association. Philadelphia, Pennsylvania, USA. June 22-26, 2001. American  
 Diabetes Association.  
 CODEN: DIAEAZ. ISSN: 0012-1797.  
 DT Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 LA English  
 ED Entered STN: 19 Sep 2001  
 Last Updated on STN: 22 Feb 2002

=> d 41, 53 55 bib ab

L7 ANSWER 41 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
 AN 2000:98732 CAPLUS  
 DN 132:150278  
 TI Methods of making protein tyrosine **phosphatase-1b**  
 (PTP-1B) deficient **mice** and their uses in drug screening for  
 obesity and diabetes therapy  
 IN Kennedy, Brian; Payette, Paul; Gresser, Michael; Ramachandran,  
 Chidambaram; Tremblay, Michel L.; Elchebly, Mounib  
 PA Merck Frosst Canada and Co., Can.; McGill University  
 SO PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000006712	A2	20000210	WO 1999-CA675	19990723 <--
	WO 2000006712	A3	20010531		
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2338643	AA	20000210	CA 1999-2338643	19990723 <--
	EP 1119614	A2	20010801	EP 1999-932587	19990723 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6605753	B1	20030812	US 2001-744383	20010123
	US 2002138862	A1	20020926	US 2001-918396	20010730
	US 2003217379	A1	20031120	US 2003-460115	20030612
PRAI	US 1998-93975P	P	19980724		
	WO 1999-CA675	W	19990723		
	US 2001-744383	A3	20010123		
AB	The present invention relates to methods of making protein tyrosine <b>phosphatase-1b</b> (PTP-1B) deficient <b>mice</b> and their uses in drug screening for obesity and diabetes therapy. The PTP-1B gene knockout <b>mice</b> (PTP-1B-/-) was made by targeted homologous recombination, which are physiol. normal but with no detectable PTP-1B				

protein. Compared to their wild-type littermates, these **mice** have half the level of circulating insulin in the fed state on a normal diet; but show a resistance to weight gain when fed a high fat, high carbohydrate diet. In glucose and insulin tolerance tests, the **mice** show an increased insulin sensitivity. The PTP-1B-/- **mice** showed increased phosphorylation of the insulin receptor in liver and muscle tissue after insulin injection in comparison to PTP-1B+/+ **mice**. These results demonstrate that PTP-1B has a major role in modulating both insulin sensitivity and fuel metabolism, thereby establishing it as a potential therapeutic target in the treatment of type 2 diabetes and obesity. Methods of making the **mice** and cell lines derived from PTP-1B-/- **mice**, and identifying **inhibitors** of the enzymic activity of PTP-1B are also provided.

L7 ANSWER 53 OF 105 MEDLINE on STN DUPLICATE 21  
AN 2000441785 MEDLINE  
DN PubMed ID: 10924321  
TI Elevated expression and activity of protein-tyrosine phosphatase 1B in skeletal muscle of insulin-resistant type II diabetic Goto-Kakizaki rats.  
AU Dadke S S; Li H C; Kusari A B; Begum N; Kusari J  
CS Department of Physiology, Tulane University School of Medicine, New Orleans, Louisiana, USA.  
NC DK 46490 (NIDDK)  
SO Biochemical and biophysical research communications, (2000 Aug 11) 274 (3) 583-9.  
Journal code: 0372516. ISSN: 0006-291X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200009  
ED Entered STN: 20000928  
Last Updated on STN: 20000928  
Entered Medline: 20000915  
AB We investigated the cellular mechanism(s) of insulin resistance associated with non-insulin dependent diabetes mellitus (NIDDM) using skeletal muscles isolated from non-obese, insulin resistant type II diabetic Goto-Kakizaki (GK) rats, a well known genetic **rat** model for type II diabetic humans. Relative to non-diabetic control rats (WKY), insulin-stimulated insulin receptor (IR) autophosphorylation and insulin receptor substrate-1 (IRS-1) tyrosine phosphorylation were significantly **inhibited** in GK skeletal muscles. This may be due to increased dephosphorylation by a protein tyrosine phosphatase (PTPase). Therefore, we measured skeletal muscle total PTPase and PTPase 1B activities in the skeletal muscles isolated from control rats (WKY) and diabetic Goto-Kakizaki (GK) rats. PTPase activity was measured using a synthetic phosphopeptide, TRDIY(P)ETDY(P)Y(P)RK, as the substrate. Basal PTPase activity was 2-fold higher ( $P < 0.001$ ) in skeletal muscle of GK rats when compared to WKY. Insulin infusion **inhibited** skeletal muscle PTPase activity in both control (26.20% of basal,  $P < 0.001$ ) and GK (25.35% of basal,  $P < 0.001$ ) rats. However, PTPase activity in skeletal muscle of insulin-stimulated GK rats was 200% higher than hormone-treated WKY controls ( $P < 0.001$ ). Immunoprecipitation of PTPase 1B from skeletal muscle lysates and analysis of the enzyme activity in immunoprecipitates indicated that both basal and insulin-stimulated PTPase 1B activities were significantly higher (twofold,  $P < 0.001$ ) in skeletal muscle of diabetic GK rats when compared to WKY controls. The increase in PTPase 1B activity in diabetic GK rats was associated with an increased expression of the PTPase 1B protein. We concluded that insulin resistance of GK rats is accompanied at least by an abnormal regulation of PTPase 1B. Elevated PTPase 1B activity through enhanced tyrosine dephosphorylation of the insulin receptor and its substrates, may lead to impaired glucose

tolerance and insulin resistance in GK rats.  
Copyright 2000 Academic Press.

L7 ANSWER 55 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:304861 CAPLUS  
DN 133:83859  
TI **PTP1B inhibition** and antihyperglycemic activity in the  
ob/ob **mouse** model of novel 11-arylbenzo[b]naphtho[2,3-d]furans  
and 11-arylbenzo[b]naphtho[2,3-d]thiophenes  
AU Li, Jie Jack; Visnick, Mike  
CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company,  
USA  
SO Chemtracts (2000), 13(4), 259-264  
CODEN: CHEMFW; ISSN: 1431-9268  
PB Springer-Verlag New York Inc.  
DT Journal; General Review  
LA English  
AB The title research of J. Wrobel et al. (1999) is reviewed with commentary  
and 3 refs.  
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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LAST RELOADED: Apr 30, 2004 (20040430/UP).

=> d 57, 66, 79 bib ab  
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, CAPLUS, ESBIOBASE' - CONTINUE?  
(Y)/N:y

L7 ANSWER 57 OF 105 CAPLUS COPYRIGHT 2004 ACS on STN  
AN 2000:331628 CAPLUS  
TI Design and synthesis of selective PTPase 1B **inhibitors** targeted  
to the treatment of type II diabetes.  
AU Primeau, John; Antane, Madelene; Adebayo, Folake; Butera, John; Caufield,  
Craig; Dietrich, Arlene; Dollings, Paul; Graceffa, Russell; Greenfield,  
Alex; Gunawan, Iwan; Gundersen, Eric; Havran, Lisa; Lennox, Joe; Li,  
Zenan; Malamas, Mike; Mayer, Scott; McDevitt, Bob; Morris, Koi; Morrison,  
Eamonn; Pan, Sherry; Wrobel, Jay; Steiner, Kurt; Moxham, Chris; Sredy,  
Janet; Sawicki, Diane; Seestaller-Wehr, Laura; Demick, Mary Ellen; Taylor,  
Joe; Baeder, William; Xu, Wei-Xin; Parris, Kevin; Katz, Alan  
CS Chemical Sciences, Wyeth-Ayerst Research, Princeton, NJ, 08543-8000, USA  
SO Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March  
26-30, 2000 (2000), MEDI-028 Publisher: American Chemical  
Society, Washington, D. C.  
CODEN: 69CLAC  
DT Conference; Meeting Abstract

LA English  
AB Based on recent data, it is now well accepted that Protein Tyrosine Phosphatase 1B plays an important role in insulin receptor signaling. This same body of data suggests that attenuation of the function of this enzyme leads to an increase in insulin sensitivity in animal models and suggests a beneficial effect in the treatment of Type II Diabetes in man. This presentation will describe the ongoing efforts at Wyeth-Ayerst Research that, beginning with both directed and high throughput screening, led to the discovery of a number of potent, small mol., PTPase 1B inhibitors. Some of the SAR studies that converted these lead structures into potent and selective agents with oral activity in animal models of human type II diabetes will also be described.

L7 ANSWER 66 OF 105 MEDLINE on STN DUPLICATE 22  
AN 1999395202 MEDLINE  
DN PubMed ID: 10464006  
TI PTP1B inhibition and antihyperglycemic activity in the ob/ob mouse model of novel 11-arylbenzo[b]naphtho[2,3-d]furans and 11-arylbenzo[b]naphtho[2,3-d]thiophenes.  
AU Wrobel J; Sredy J; Moxham C; Dietrich A; Li Z; Sawicki D R; Seestaller L; Wu L; Katz A; Sullivan D; Tio C; Zhang Z Y  
CS Wyeth-Ayerst Research, Inc., CN 8000, Princeton, New Jersey 08543-8000, USA.  
SO Journal of medicinal chemistry, (1999 Aug 26) 42 (17) 3199-202.  
Journal code: 9716531. ISSN: 0022-2623.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199909  
ED Entered STN: 19991005  
Last Updated on STN: 19991005  
Entered Medline: 19990920

L7 ANSWER 79 OF 105 MEDLINE on STN DUPLICATE 28  
AN 1999018625 MEDLINE  
DN PubMed ID: 9801817  
TI Potent non-peptidyl inhibitors of protein tyrosine phosphatase 1B.  
CM Erratum in: Bioorg Med Chem 1998 Nov;6(11):2235  
AU Taylor S D; Kotoris C C; Dinaut A N; Wang Q; Ramachandran C; Huang Z  
CS Department of Chemistry, Erindale College, University of Toronto, Mississauga, Ontario, Canada.. staylor@credit.erin.utoronto.ca  
SO Bioorganic & medicinal chemistry, (1998 Sep) 6 (9) 1457-68.  
Journal code: 9413298. ISSN: 0968-0896.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199901  
ED Entered STN: 19990128  
Last Updated on STN: 20000303  
Entered Medline: 19990112  
AB The development of inhibitors of protein tyrosine phosphatases (PTPs) has recently been the subject of intensive investigation due to their potential as chemotherapeutics and as tools for studying signal transduction pathways. Here we report the evaluation of a variety of small molecule, non-peptidyl inhibitors of protein tyrosine phosphatase 1B (PTP1B), bearing the alpha, alpha-difluoromethylphosphonic acid (DFMP) group, a non-hydrolyzable phosphate mimetic. A series of phenyl derivatives bearing a single DFMP group were initially surveyed. In general, these were not significantly

more potent **inhibitors** than the parent compound, alpha, alpha-difluorobenzylphosphonic acid, with the exception being the meta-phenyl substituted species which decreased the IC50 by approximately 17-fold relative to alpha, alpha-difluorobenzylphosphonic acid. However, certain compounds bearing two DFMP moieties were very potent **inhibitors**. Some of these are among the most potent small molecule **inhibitors** of any PTP reported to date with the best one exhibiting a Ki of 1.5 microM. The structural basis for these results are discussed. One of the bis-DFMP **inhibitors** was examined in detail and it was found that the fluorines were essential for potent **inhibition**. **Inhibition** was independent of pH between pH 5.5-7.2 suggesting that both the mono and dianionic forms of the individual DFMP groups bind equally well. The trends observed in the **inhibitory** potency of these compounds with **PTP1B** were very similar to the trends observed by other workers on the K(m)'s of the analogous phenylphosphate substrates with **rat PTP1**. This indicates that studies of non-peptidyl substrates with **rat PTP1** can be used as a guide for the development of human **PTP1B** **inhibitors**.

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